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File: USPT

Nov 23, 1993

DOCUMENT-IDENTIFIER: US 5264221 A

TITLE: Drug-containing protein-bonded liposomeAbstract Text (1):

A drug-containing protein-bonded liposome comprising a liposome containing a drug and having maleimide residues on its surface, and a protein and residues of a compound having a polyalkylene glycol moiety, bonded via respective thiol groups to the maleimide residues.

Brief Summary Text (1):

The present invention relates to selective chemotherapeutic drugs for various diseases including cancer. More particularly, it relates to a drug-containing protein-bonded liposome.

Brief Summary Text (7):

Thus, the present invention provides a drug-containing protein-bonded liposome comprising a liposome containing a drug and having maleimide residues on its surface, and a protein and residues of a compound having a polyalkylene glycol moiety, bonded via respective thiol groups to the maleimide residues.

Detailed Description Text (23):

(6) Method of Use of the Drug-Containing Protein-Bonded Liposome

Detailed Description Text (24):

The drug-containing protein-bonded liposome thus obtained, such as an adriamycin-containing antibody-bonded PEG-modified liposome, may be formulated into a drug by a conventional method such as a dehydration method (Japanese PCT Publication No. 502348/1990), a method wherein a stabilizer is added to form a liquid formulation (Japanese Unexamined Patent Publication No. 9331/1989) or a freeze-drying method (Japanese Unexamined Patent Publication No. 9931/1989).

Current US Original Classification (1):

424/450

CLAIMS:

1. A drug containing, protein-bonded liposome, which comprises a liposome containing a drug, said liposome having maleimide groups on the surface thereof, wherein a portion of the maleimide groups are bonded to a thiol group-containing protein and a remaining portion of the maleimide groups are bonded to a thiol group-containing polyethylene glycol moiety; said liposome comprising phosphatidyl choline, cholesterol and maleimide-modified phosphatidyl ethanolamine.
2. The drug-containing, protein-bonded liposome of claim 1, wherein the protein is selected from the group consisting of an antibody, FGF and EGF.
3. The drug-containing, protein-bonded liposome of claim 2, wherein said protein is an antibody selected from the group consisting of animal polyclonal antibodies,

mouse monoclonal antibodies, human-mouse chimeric antibodies and human monoclonal antibodies.

4. The drug-containing, protein-bonded liposome of claim 3, wherein said protein is a human monoclonal antibody.

5. The drug-containing, protein-bonded liposome of claim 1, wherein the liposome comprises dipalmitoylphosphatidyl choline, cholesterol and maleimide-modified dipalmitoylphosphatidyl ethanolamine.

6. The drug-containing, protein-bonded liposome of claim 5, wherein the maleimide-modified dipalmitoylphosphatidyl ethanolamine is obtained by reacting N-(.epsilon.-maleimidocaproyloxy) succinimide and dipalmitoylphosphatidyl ethanolamine.

7. The drug-containing, protein-bonded liposome of claim 1, wherein the thiol group-containing protein having maleimide groups bonded thereto is obtained by reacting maleimide residues on the liposome surface and a thiol group-containing protein.

8. The drug-containing, protein-bonded liposome of claim 1, wherein said thiol-group containing polyethylene glycol moiety having maleimide groups bonded thereto is obtained by reacting maleimide residues on the liposome surface and a thiol-group containing polyethylene glycol.

9. The drug-containing, protein-bonded liposome of claim 1, wherein said drug comprises an antitumor drug, a .beta.-lactam antibiotic, a toxin, an aminoglycoside, antisense RNA or actinoplan.

10. The drug-containing, protein-bonded liposome of claim 9, wherein the antitumor drug is selected from the group consisting of adriamycin, daunomycin, mitomycin, cisplatin, vincristine, epirubicin, methotrexate, 5-FU and aclacinomycin.

11. The drug containing, protein-bonded liposome of claim 9, wherein said aminoglycoside is gentamicin.

12. The drug containing, protein-bonded liposome of claim 9, wherein said .beta.-lactam antibiotic is sulpenisillin.

13. The drug containing, protein-bonded liposome of claim 9, wherein said toxin is ricin A or diphtheria toxin.

14. The drug containing, protein-bonded liposome of claim 9, wherein said antisense RNA is antisense RNA against HIV or ras gene.

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File: USPT

Nov 23, 1993

US-PAT-NO: 5264221

DOCUMENT-IDENTIFIER: US 5264221 A

TITLE: Drug-containing protein-bonded liposome

DATE-ISSUED: November 23, 1993

INVENTOR-INFORMATION:

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US-CL-CURRENT: 424/450; 428/402.2, 436/829, 530/812

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